# General

## Guideline Title

Best evidence statement (BESt). Oral anxiolytic medication prior to ambulatory healthcare encounters for individuals with special developmental and behavioral challenges.

## Bibliographic Source(s)

Cincinnati Children's Hospital Medical Center. Best evidence statement (BESt). Oral anxiolytic medication prior to ambulatory healthcare encounters for individuals with special developmental and behavioral challenges. Cincinnati (OH): Cincinnati Children's Hospital Medical Center; 2011 Mar 10. 15 p. [31 references]

## Guideline Status

This is the current release of the guideline.

# Recommendations

## Major Recommendations

The strength of the recommendation (strongly recommended, recommended, or no recommendation) and the quality of evidence (1a-5) are defined at the end of the "Major Recommendations" field.

1. It is recommended that the following parameters be taken into account when selecting the specific anxiolytic medication.
    - Patient's current medications (with specific attention to drug-drug interactions)
    - Contraindications in the medical and behavioral history, and individual patient challenges
    - Specific procedure/visit considerations (e.g., invasiveness, duration)

    (Local Consensus, 2011 [5])

2. It is recommended that the selected anxiolytic medication be trialed by the family prior to the day of the healthcare encounter, when possible, to assess appropriate timing of dose and to observe for possible side effects. The lowest possible therapeutic dose of the anxiolytic medication used is preferred to avoid adverse effects (Local Consensus, 2011 [5]). (See Appendix 3 [section D] in the original guideline document.)
3. It is recommended that the pharmacological intervention be:
    - First line: clonazepam (Local Consensus, 2011 [5])

      Note: If a patient takes a different medication for maintenance which would also be effective for anxiety, an alternate for first line pharmacological intervention would be to increase dosage of maintenance medication (Local Consensus, 2011 [5]).

    - Second line: risperidone (Veser et al., 2006 [2b]; Crosland et al., 2003 [4b])

- Third line: lorazepam (adolescents age 13 and older) (Veser et al., 2006 [2b]; Battaglia et al., 1997 [2b]).

See the table in the original guideline document for dosages. The lowest possible therapeutic dose of the anxiolytic medication used is preferred to avoid adverse effects.

Definitions:

Table of Evidence Levels

| Quality Level | Definition |
|---|---|
| 1a† or 1b† | Systematic review, meta-analysis, or meta-synthesis of multiple studies |
| 2a or 2b | Best study design for domain |
| 3a or 3b | Fair study design for domain |
| 4a or 4b | Weak study design for domain |
| 5 | Other: General review, expert opinion, case report, consensus report, or guideline |

†a = good quality study; b = lesser quality study

Table of Recommendation Strength

| Strength | Definition |
|---|---|
| "Strongly recommended" | There is consensus that benefits clearly outweigh risks and burdens (or visa-versa for negative recommendations). |
| "Recommended" | There is consensus that benefits are closely balanced with risks and burdens. |
| No recommendation made | There is lack of consensus to direct development of a recommendation. |
| Dimensions: In determining the strength of a recommendation, the development group makes a considered judgment in a consensus process that incorporates critically appraised evidence, clinical experience, and other dimensions as listed below. | |
| 1. Grade of the Body of Evidence (see note above)<br>2. Safety/Harm<br>3. Health benefit to patient (direct benefit)<br>4. Burden to patient of adherence to recommendation (cost, hassle, discomfort, pain, motivation, ability to adhere, time)<br>5. Cost-effectiveness to healthcare system (balance of cost/savings of resources, staff time, and supplies based on published studies or onsite analysis)<br>6. Directness (the extent to which the body of evidence directly answers the clinical question [population/problem, intervention, comparison, outcome])<br>7. Impact on morbidity/mortality or quality of life | |

## Clinical Algorithm(s)

None provided

# Scope

## Disease/Condition(s)

Anxiety in children with special developmental and behavioral challenges

## Guideline Category

Treatment

## Clinical Specialty

Emergency Medicine

Family Practice

Internal Medicine

Pediatrics

Psychiatry

Psychology

## Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

## Guideline Objective(s)

To evaluate in children with special developmental and behavioral challenges, who present for an ambulatory healthcare encounter and have significant anxiety that may disrupt their visit, if the use of an oral anxiolytic medication before the healthcare encounter, in comparison to either forced compliance, an incomplete healthcare visit, sedation, or general anesthesia, allows for improved experience and completion of care with acceptable side effects

## Target Population

Inclusion Criteria

- Age 3 years and older
- Patients with special developmental and behavioral challenges who have difficulty tolerating ambulatory healthcare encounters
- Able to take oral medications
- Unable to tolerate healthcare encounters even with non-pharmacological support interventions

Exclusion Criteria

Patients with contraindications based on history and physical examination, including:

- Major craniofacial airway abnormalities
- Obstructive sleep apnea
- Major cardiac anomalies

## Interventions and Practices Considered

1. Assessment of current medications, contraindications, behavioral challenges
2. Specific procedural/visit considerations (invasiveness, duration)
3. Pharmacological therapy
    - Clonazepam (first line)
    - Risperidone (second line)
    - Lorazepam (third line)
4. Increased dosage of current maintenance medication (if applicable)
5. Trial of selected anxiolytic medication
    - Assessment of timing, dose, and side effects prior to day of healthcare encounter

## Major Outcomes Considered

- Experience and completion of care
- Side effects

# Methodology

## Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

## Description of Methods Used to Collect/Select the Evidence

Search Strategy

1. Initial Searches
   Databases: CINAHL, MEDLINE, PSYCHINFO
   All dates through December, 2008
   Keywords: autism, developmental disabilities, pervasive developmental disability, patient compliance, preoperative, anxiety, medication, pre-medication, clonidine, anti-psychotic, benzodiazepine, anxiolytics, side effects

   Database: MEDLINE
   All dates through April 20, 2009
   *Antipsychotic Agents/ or atypical antipsychotics.mp AND
   (premedication.mp OR anxiolytic.mp OR Anti-Anxiety Agents/ OR chemical restraint.mp)
   Filtered for child age 0 to 18 years and English language

2. Additional Searches
   Databases: CINAHL, MEDLINE, PSYCHINFO
   All Dates through April 20, 2009
   Keywords: buspirone, chloral hydrate, clonidine, haliperidone

   Database: MEDLINE
   All Dates through May, 2010

    a. Clonazepam OR risperidone OR lorazepam
    b. Filtered for English language only and children age 0 to 18 years
    c. AND (airway OR cardiov$ OR blood pressure OR tachycardia OR safety)

- Filtered for (autism OR ex Autism Disorder/ OR exp Disabled Children)
- Filtered for (anx$ or exp Anxiety/ OR Anti-Anxiety Agents/ OR Dental Anxiety)

d. Separate search for a AND b above AND (overdose$ or accidental ingestion or poison control center$)

3. Additional articles identified from reference lists and clinicians

A separate search of the literature was also conducted to specifically address safety concerns with use of the three recommended medications: clonazepam, risperidone, and lorazepam.

## Number of Source Documents

Not stated

## Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

## Rating Scheme for the Strength of the Evidence

Table of Evidence Levels

| Quality Level | Definition |
|---|---|
| 1a† or 1b† | Systematic review, meta-analysis, or meta-synthesis of multiple studies |
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| 3a or 3b | Fair study design for domain |
| 4a or 4b | Weak study design for domain |
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†a = good quality study; b = lesser quality study

## Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

## Description of the Methods Used to Analyze the Evidence

Not stated

## Methods Used to Formulate the Recommendations

Expert Consensus

## Description of Methods Used to Formulate the Recommendations

Not stated

## Rating Scheme for the Strength of the Recommendations

Table of Recommendation Strength

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|---|---|
| "Strongly recommended" | There is consensus that benefits clearly outweigh risks and burdens (or visa-versa for negative recommendations). |
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## Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

## Method of Guideline Validation

Peer Review

## Description of Method of Guideline Validation

This Best Evidence Statement has been reviewed against quality criteria by two independent reviewers from the Cincinnati Children's Hospital Medical Center (CCHMC) Evidence Collaboration.

# Evidence Supporting the Recommendations

## References Supporting the Recommendations


Battaglia J, Moss S, Rush J, Kang J, Mendoza R, Leedom L, Dubin W, McGlynn C, Goodman L. Haloperidol, lorazepam, or both for psychotic agitation? A multicenter, prospective, double-blind, emergency department study. Am J Emerg Med. 1997 Jul;15(4):335-40. PubMed

Crosland KA, Zarcone JR, Lindauer SE, Valdovinos MG, Zarcone TJ, Hellings JA, Schroeder SR. Use of functional analysis methodology in the evaluation of medication effects. J Autism Dev Disord. 2003 Jun;33(3):271-9. PubMed

Veser FH, Veser BD, McMullan JT, Zealberg J, Currier GW. Risperidone versus haloperidol, in combination with lorazepam, in the treatment of acute agitation and psychosis: a pilot, randomized, double-blind, placebo-controlled trial. J Psychiatr Pract. 2006 Mar;12(2):103-8. PubMed

### Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

## Benefits/Harms of Implementing the Guideline Recommendations

### Potential Benefits

The following benefits from implementation of these recommendations are predicted:

- A more productive and thorough appointment
- Decreased distress during appointment
- Improved experience of care
- Improved reliability for completion of follow-up appointments.

Non-pharmacological methods are safest, and patients are not considered eligible for anxiolytic recommendations unless it has been observed that the patient is unable to tolerate healthcare encounters even with non-pharmacological support interventions. The potential benefit of preprocedural anxiolytic medications required to accomplish medical encounters in this population is revealed both in terms of improved patient safety and in minimization of resource expenditure when compared to the alternatives of non-oral, sedative, or general anesthetic medications. Use of those alternatives requires higher acuity medical resources, such as the use of the operating room environment and/or the need for more intensive monitoring.

### Potential Harms

Safety concerns are a key driver in the selection of medications for pre-procedural anxiolytic medications for this population. Side effects and potential adverse effects of medication administration are always balanced against the benefits of their use and alternatives to their use. See the table in the original guideline document for potential side effects and adverse effects for recommended medications, and see the discussion in the original guideline document for safety concerns for specific medications not included in the recommendations. See also Appendix 3 in the original guideline document for safety guidance for use of oral anxiolytic medication prior to healthcare encounters.

## Contraindications

### Contraindications

Patient contraindications for oral anxiolytic use include (but are not limited to):

- Major craniofacial airway abnormalities
- Obstructive sleep apnea
- Major cardiac anomalies

## Qualifying Statements

### Qualifying Statements

This Best Evidence Statement addresses only key points of care for the target population; it is not intended to be a comprehensive practice guideline. These recommendations result from review of literature and practices current at the time of their formulation. This Best Evidence Statement does not preclude using care modalities proven efficacious in studies published subsequent to the current revision of this document. This document is not intended to impose standards of care preventing selective variances from the recommendations to meet the specific and unique requirements of individual patients. Adherence to this Statement is voluntary. The clinician in light of the individual circumstances presented by the patient must make the ultimate judgment regarding the priority of any specific procedure.

# Implementation of the Guideline

## Description of Implementation Strategy

An implementation strategy was not provided.

## Implementation Tools

Patient Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

# Institute of Medicine (IOM) National Healthcare Quality Report Categories

## IOM Care Need

Living with Illness

## IOM Domain

Effectiveness

# Identifying Information and Availability

## Bibliographic Source(s)

Cincinnati Children's Hospital Medical Center. Best evidence statement (BESt). Oral anxiolytic medication prior to ambulatory healthcare encounters for individuals with special developmental and behavioral challenges. Cincinnati (OH): Cincinnati Children's Hospital Medical Center; 2011 Mar 10. 15 p. [31 references]

## Adaptation

Not applicable: The guideline was not adapted from another source.

## Date Released

2011 Mar 10

## Guideline Developer(s)

Cincinnati Children's Hospital Medical Center - Hospital/Medical Center

## Source(s) of Funding

Cincinnati Children's Hospital Medical Center

## Guideline Committee

Not stated

## Composition of Group That Authored the Guideline

*Team Leaders*: Brad Dixon, MD, Research Asst. Professor, Division of Nephrology & Hypertension, & parent of a child with autism spectrum disorder; Gail Klayman, MEd, CCLS, Coordinator, Adaptive Care Team, Center for Professional Excellence and Business Integration; Judy Reinhold, RN, MSN, CPNP, Nurse Practitioner, The Kelly O'Leary Center for Autism, Division of Developmental & Behavioral Pediatrics

*Team Members*: Roxane Anderson, RN, CPNP, Nurse Practitioner, Department of Anesthesia; Gary Geis, MD, Assistant Professor, Division of Emergency Medicine; Brad McCrory, PharmD, Clinical Pharmacy Specialist, Division of Pharmacy; Monica Meier, RN, Holistic Health Specialist, Integrative Care; Jennifer Staab, MS, CCLS, Adaptive Care Team, Center for Professional Excellence and Business Integration; Eric Wittkugel, MD, Associate Professor, Department of Anesthesia; Michelle Zimmer, MD, Developmental Pediatrician, Division of Developmental & Behavioral Pediatrics

*Anderson Center Support*: Eloise Clark, MPH, MBA, Lead Guidelines Program Administrator, Anderson Center for Health Systems Excellence

*Ad Hoc Advisors*: Jessica Bechtold, MS, Project Manager, Division of Access Services & Family Relations; Beth Beineke, RN, Nurse, Pediatric Acute Care Unit; Randall Bond, MD, Emergency Medicine, CCHMC Pharmacy and Therapeutics Committee; Murray Dock, DDS, Associate Professor, Division of Pediatric Dentistry; Nancy Hagerman, MD, Assistant Professor, Department of Anesthesia; Stacy Levi, RN, Nurse, Same Day Surgery; Ron Levin, MD, Associate Professor, Center for Infants and Children with Special Needs; David J. Schonfeld, MD, Director, Division of Developmental and Behavioral Pediatrics

## Financial Disclosures/Conflicts of Interest

Not stated

## Guideline Status

This is the current release of the guideline.

## Guideline Availability

Electronic copies: Available from the Cincinnati Children's Hospital Medical Center .

Print copies: For information regarding the full-text guideline, print copies, or evidence-based practice support services contact the Cincinnati Children's Hospital Medical Center Health James M. Anderson Center for Health Systems Excellence at EBDMInfo@cchmc.org.

## Availability of Companion Documents

The following are available:

- Judging the strength of a recommendation. Cincinnati (OH): Cincinnati Children's Hospital Medical Center; 2008 Jan. 1 p. Available from the Cincinnati Children's Hospital Medical Center .
- Grading a body of evidence to answer a clinical question. Cincinnati (OH): Cincinnati Children's Hospital Medical Center; 1 p. Available from the Cincinnati Children's Hospital Medical Center .
- Table of evidence levels. Cincinnati (OH): Cincinnati Children's Hospital Medical Center; 2008 Feb 29. 1 p. Available from the Cincinnati Children's Hospital Medical Center .

Print copies: For information regarding the full-text guideline, print copies, or evidence-based practice support services contact the Cincinnati Children's Hospital Medical Center Health James M. Anderson Center for Health Systems Excellence at EBDMInfo@cchmc.org.

## Patient Resources

The following is available:

- Lorazepam. Your child's health. Cincinnati (OH): Cincinnati Children's Hospital Medical Center; 2010 Dec. 1 p. Available from the Cinicnnati Children's Hospital Medical Center Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

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